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PATENT
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AMENDMENTS TO THE CLAIMS:

Please amend claims 1, 3, 4, 6, 25 and 42 as follows:

Please cancel claims 20, 21, 23, 24, 26-40, and 44-51 without prejudice.

Please add new claims 52-73:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. **(currently amended)** A method of inhibiting HCV replication ~~of one or more viruses~~ in an individual comprising administering to said individual a composition comprising an arginine deiminase bonded to polyethylene glycol in an amount effective to inhibit ~~viral~~ HCV replication in said individual.

2. **(original)** The method of claim 1 further comprising the step of administering to said individual one or more compounds selected from the group consisting of antibiotics, anti-virals, antifungals, and anti-protozoan drugs.

3. **(currently amended)** The method of claim 1 further comprising the step of administering to said individual one or more conventional antiviral compounds ~~other anti-viral compounds~~.

4. **(currently amended)** The method of claim 2 wherein said anti-viral compounds are one or more of azidovudine (AZT), didanosine (dideoxyinosine, ddI), d4T, zalcitabine (dideoxycytosine, ddC), nevirapine, lamivudine (epivir, 3TC), saquinavir (Invirase), ritonavir (Norvir), indinavir (Crixivan), delavirdine (Rescriptor), pegylated (PEG) interferon-α (IFN), or ribavirin .

5. **(original)** The method of claim 1 wherein said composition is administered intramuscularly, intradermally, or intraperitoneally.

6. **(currently amended)** The method of claim 1 wherein said composition comprising an arginine deiminase bonded to polyethylene glycol is effective at a

concentration of less than ~~about~~ 1 mM to inhibit viral replication by at least 50% ~~in greater than 50% of cells in an assay to measure viral replication~~.

7. **(original)** The method of claim 1 wherein the amount of arginine deiminase bonded to polyethylene glycol effective to inhibit viral replication is between about 40 IU/m^2 and about 160 IU/m^2 per week.

8. **(original)** The method of claim 1 wherein the amount of arginine deiminase bonded to polyethylene glycol effective to inhibit viral replication is about 160 IU/m^2 per week.

9. **(original)** The method of claim 1 wherein the amount of arginine deiminase bonded to polyethylene glycol effective to inhibit viral replication lowers plasma arginine levels to less than 5 μM.

10. **(original)** The method of claim 1 wherein the arginine deiminase is covalently bonded via a linking group to polyethylene glycol, wherein each of said polyethylene glycol molecules has a molecular weight of about 10,000 to about 30,000.

11. **(original)** The method of claim 1 wherein each of said polyethylene glycol molecules has a molecular weight of about 20,000.

12. **(original)** The method of claim 10 wherein the linking group is selected from the group consisting of a succinimide group, an amide group, an imide group, a carbamate group, an ester group, an epoxy group, a carboxyl group, a hydroxyl group, a carbohydrate, a tyrosine group, a cysteine group, and a histidine group, and combinations thereof.

13. **(original)** The method of claim 10 wherein the linking group is succinimidyl succinate.

14. **(original)** The method of claim 1 wherein from about 7 to about 15 polyethylene glycol molecules are bonded to arginine deiminase.

15. **(original)** The method of claim 1 wherein from about 9 to about 12 said polyethylene glycol molecules are bonded to arginine deiminase.

16. **(original)** The method of claim 1 wherein said arginine deiminase is derived from a microorganism of the genus *Mycoplasma*.

17. **(original)** The method of claim 16 wherein said microorganism is selected from the group consisting of *Mycoplasma arginini*, *Mycoplasma hominus*, *Mycoplasma arthritides* and combinations thereof.

18. **(original)** The method of claim 1 wherein the arginine deiminase has an amino acid sequence of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 13, 14, 15, 16, 17, 18, 19, 20 or 21.

19. **(original)** The method of claim 1 wherein the arginine deiminase has an amino acid sequence of SEQ ID NO: 1 or 4.

20. **(cancelled)** The method of claim 1 wherein the virus is a hepatitis virus.

21. **(cancelled)** The method of claim 1 wherein the virus is HCV.

22. **(original)** The method of claim 1 wherein the virus is HCV1b.

23. **(cancelled)** A method of treating an individual who is suspected of having been exposed to one or more viruses comprising the step of administering to said individual an amount of a composition comprising an arginine deiminase bonded to polyethylene glycol effective to inhibit viral replication in said individual.

24. **(cancelled)** A method of inhibiting viral replication in an individual at risk for one or more viruses comprising administering to said individual an amount of a composition comprising an arginine deiminase bonded to polyethylene glycol effective to inhibit viral replication in said individual.

25. **(currently amended)** A method of inhibiting ~~viral~~ HCV replication in an individual who has been identified as having been infected with ~~one or more viruses~~ HCV comprising administering to said individual an amount of a composition comprising an arginine deiminase bonded to polyethylene glycol effective to inhibit ~~viral~~ HCV replication in said individual.

26. **(cancelled)** A method of concurrently treating a tumor and inhibiting replication of one or more viruses in an individual, said method comprising the step of administering a therapeutically or prophylactically effective amount of a composition comprising arginine deiminase covalently bonded via a linking group to polyethylene glycol to said individual effective to inhibit tumor growth and inhibit viral replication.

27. **(cancelled)** The method of claim 26 wherein the individual has been identified as having been infected with one or more viral infections prior to administration of the composition.

28. **(cancelled)** The method of claim 26 wherein the tumor is melanoma, sarcoma, or hepatoma.

29. **(cancelled)** The method of claim 26 wherein the tumor is hepatocellular carcinoma.

30. **(cancelled)** The method of any one of claims 23-27 wherein the virus is a hepatitis virus.

31. **(cancelled)** The method of any one of claims 23-27 wherein said virus is HCV.

32. **(cancelled)** The method of claim 26 wherein said tumor is hepatocellular carcinoma and said virus is HCV.

33. **(cancelled)** A method for modulating nitric oxide levels in an individual comprising administering an amount of an arginine deiminase bonded to polyethylene glycol effective to modulate nitric oxide to said individual.

34. **(cancelled)** The method of claim 33 wherein the arginine deiminase is covalently bonded via a linking group to polyethylene glycol, wherein each of said polyethylene glycol molecules has a molecular weight of about 10,000 to about 30,000.

35. **(cancelled)** The method of claim 33 wherein each of said polyethylene glycol molecules has a molecular weight of about 20,000.

36. **(cancelled)** The method of claim 34 wherein the linking group is one or more of a succinimide group, an amide group, an imide group, a carbamate group, an ester group, an epoxy group, a carboxyl group, a hydroxyl group, a carbohydrate, a tyrosine group, a cysteine group or a histidine group.

37. **(cancelled)** The method of claim 34 wherein from about 7 to about 12 polyethylene glycol molecules are bonded to arginine deiminase.

38. **(cancelled)** The method of claim 33 wherein said arginine deiminase is derived from a microorganism of the genus *Mycoplasma*.

39. **(cancelled)** A method to determine the sensitivity of viral replication to modulating levels of arginine comprising:

(a) contacting a sample comprising one or more viruses with a composition comprising arginine deiminase bonded to polyethylene glycol; and

(b) comparing levels of viral replication in the presence and absence of the composition comprising arginine deiminase bonded to polyethylene glycol;

wherein decreased viral replication in samples contacted with arginine deiminase is indicative of viral sensitivity to arginine deiminase.

40. **(cancelled)** A method to determine the sensitivity of viral replication to modulating levels of nitric oxide comprising:

(a) contacting a sample comprising one or more viruses with a composition comprising arginine deiminase bonded to polyethylene glycol; and

(b) comparing levels of viral replication in the presence and absence of the composition comprising arginine deiminase bonded to polyethylene glycol,

wherein decreased viral replication in samples contacted with arginine deiminase is indicative of viral sensitivity to nitric oxide.

41. **(original)** The method of any one of claims 2 or 3 wherein said compound is administered to said individual simultaneously with the administration of said composition comprising arginine deiminase bonded to polyethylene glycol.

42. **(currently amended)** A method of selectively inhibiting HCV ~~viral~~ replication in an individual in need thereof comprising administering a therapeutically or

prophylactically effective amount of a composition comprising an arginine deiminase bonded to polyethylene glycol to said individual.

43. **(cancelled)** The method of claim 42 wherein the virus is HCV.

44. **(cancelled)** A method for improving liver function in an individual comprising administering a therapeutically effective amount of a composition comprising arginine deiminase bonded to polyethylene glycol to said individual.

45. **(cancelled)** The method of claim 44 wherein liver function is assessed using the Child-Pugh scale or the Mayo End-stage Liver Disease score.

46. **(cancelled)** The method of claim 44 wherein liver function is assessed by measuring at least one marker of liver function, wherein the marker is billrubin, albumin, prothrombin time, presence of ascites, or grade of enephalopathy.

47. **(cancelled)** The method of claim 44 wherein the liver function of said individual prior to administration of the composition comprising arginine deiminase bonded to polyethylene glycol is Child-Pugh level A.

48. **(cancelled)** The method of claim 44 wherein the liver function of said individual prior to administration of the composition comprising arginine deiminase bonded to polyethylene glycol is Child-Pugh level B.

49. **(cancelled)** The method of claim 44 wherein the liver function of said individual prior to administration of the composition comprising arginine deiminase bonded to polyethylene glycol is Child-Pugh level C.

50. **(cancelled)** A method for identifying an individual as susceptible to arginine deprivation therapy, said individual identified as having one or more viral infections, the method comprising:

a) obtaining a sample comprising one or more viruses from the individual; and

b) comparing viral replication in the sample contacted with a composition comprising arginine deiminase bonded to polyethylene glycol under conditions suitable for viral replication to viral replication in the sample in the absence of a composition comprising arginine deiminase bonded to polyethylene glycol, wherein an inhibition of

viral replication of at least 40% in said sample is indicative of an individual who is a candidate for arginine deprivation therapy and an inhibition of viral replication of less than 40% is indicative of an individual who is not a candidate for arginine deprivation therapy.

51. **(cancelled)** A method of treating one or more viruses in an individual comprising:

a) determining if the individual is a candidate for arginine deprivation therapy according to claim 50;

b) treating the individual with arginine deprivation therapy if the individual is a candidate for arginine deprivation therapy; and

c) treating the individual with conventional antiviral treatment if the individual is not a candidate for arginine deprivation therapy.

52. **(new)** The method of claim 3 wherein the one or more conventional antiviral medicaments are selected from the group consisting of cyclovir, famciclovir, valacyclovir, ribavirin, interferon or beta globulin.

53. **(new)** A method of reducing HCV viral titer in an individual comprising administering to said individual a composition comprising an arginine deiminase bonded to polyethylene glycol in an amount effective to reduce HCV viral titer in said individual.

54. **(new)** The method of claim 53 further comprising the step of administering to said individual one or more conventional antiviral compounds.

55. **(new)** The method of claim 53 wherein said composition is administered intramuscularly, intradermally, or intraperitoneally.

56. **(new)** The method of claim 53 wherein said composition comprising an arginine deiminase bonded to polyethylene glycol is effective at a concentration of less than 1 mM to reduce HCV viral titer by at least 50%.

57. **(new)** The method of claim 53 wherein the amount of arginine deiminase bonded to polyethylene glycol effective to reduce HCV viral titer is between about 40 IU/m^2 and about 160 IU/m^2 per week.

58. (new) The method of claim 53 wherein the amount of arginine deiminase bonded to polyethylene glycol effective to reduce HCV viral titer is about 160 IU/m^2 per week.

59. (new) The method of claim 53 wherein the amount of arginine deiminase bonded to polyethylene glycol effective to reduce HCV viral titer lowers plasma arginine levels to less than 5 μM.

60. (new) The method of claim 53 wherein the arginine deiminase is covalently bonded via a linking group to polyethylene glycol, wherein each of said polyethylene glycol molecules has a molecular weight of about 10,000 to about 30,000.

61. (new) The method of claim 53 wherein each of said polyethylene glycol molecules has a molecular weight of about 20,000.

62. (new) The method of claim 60 wherein the linking group is selected from the group consisting of a succinimide group, an amide group, an imide group, a carbamate group, an ester group, an epoxy group, a carboxyl group, a hydroxyl group, a carbohydrate, a tyrosine group, a cysteine group, and a histidine group, and combinations thereof.

63. (new) The method of claim 60 wherein the linking group is succinimidyl succinate.

64. (new) The method of claim 53 wherein from about 7 to about 15 polyethylene glycol molecules are bonded to arginine deiminase.

65. (new) The method of claim 53 wherein from about 9 to about 12 said polyethylene glycol molecules are bonded to arginine deiminase.

66. (new) The method of claim 53 wherein said arginine deiminase is derived from a microorganism of the genus *Mycoplasma*.

67. (new) The method of claim 66 wherein said microorganism is selected from the group consisting of *Mycoplasma arginini*, *Mycoplasma hominus*, *Mycoplasma arthritides* and combinations thereof.

68. **(new)** The method of claim 53 wherein the arginine deiminase has an amino acid sequence of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 13, 14, 15, 16, 17, 18, 19, 20 or 21.

69. **(new)** The method of claim 53 wherein the arginine deiminase has an amino acid sequence of SEQ ID NO: 1 or 4.

70. **(new)** The method of claim 53 wherein the virus is HCV1b.

71. **(new)** The method of claim 54 wherein the one or more conventional antiviral medicaments are selected from the group consiting of cyclovir, famciclovir, valacyclovir, ribavirin, interferon or beta globulin.

72. **(new)** The method of claim 53 wherein the amount of arginine deiminase bonded to polyethylene glycol administered to the individual is about 200 IU/m^2 per week.

73. **(new)** The method of claim 1 wherein the amount of arginine deiminase bonded to polyethylene glycol administered to the individual is about 200 IU/m^2 per week.